# Research Roundtable Summary

11

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## Effects at Age 5 of an Intervention Program for Low Birthweight Premature Infants

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Cecelia McCarton, M.D.

Director
L.I.F.E. Program
Rose F. Kennedy Center


**Reaction**


Howard Bauchner, M.D.

Associate Professor
Department of Pediatrics
Boston University School of Medicine



U.S. Department of Health & Human Services
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For more information, please contact Michelle Keyes-Welch, NCEMCH, (703) 524-7802.

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## About This Series

The Research Roundtable Series, sponsored by the Maternal and Child Health Bureau (MCHB), disseminates the results of MCHB-funded research to policymakers, researchers, and practitioners in the public and private sectors. The results of these projects influence future service, research, and policy development. The Research Roundtable sessions provide an opportunity for researchers to discuss their findings with policymakers, MCH program directors, service providers, and other health professionals.

The Maternal and Child Health Research Program is directed by Dr. Gontran Lamberty and administered through the Division of Systems, Education and Analysis, Maternal and Child Health Bureau, Health Resources and Services Administration (HRSA). HRSA is a component of the Public Health Service (PHS), part of the U.S. Department of Health and Human Services (DHHS). The purpose of the research program is to support applied research relating to maternal and child health services that shows promise of making a substantial contribution to the advancement of those services.

## Introduction

Dr. Cecelia McCarton is a professor in the Department of Pediatrics at the Albert Einstein College of Medicine. She is also director of the L.I.F.E. (Low Birthweight Infant Followup and Evaluation) Program at the Rose F. Kennedy Center in New York. Reaction was provided by Dr. Howard Bauchner, an associate professor of pediatrics at Boston University School of Medicine, and director of the Division of General Pediatrics at Boston City Hospital.

## Presentation

The Infant Health and Development Program (IHDP) is the first multicenter, randomized controlled trial of an intervention for low birthweight infants (newborns who weigh 2,500 grams or less and are born at 37 or fewer weeks' gestation). These infants are known to be at high risk for developmental dysfunction and school failure. The 3-year intervention consisted of early child development programs and family services. In presenting the study, Dr. McCarton first reviewed developmental issues relating to low birthweight infants and then discussed the findings of the study at the children's age 3 and age 5.

*Developmental Issues Relating to Low Birthweight Infants*

Dr. McCarton noted that low birthweight infants have developmental difficulties both at and after birth. As a group, they have a large number of neurological problems, primarily in the realm of cerebral palsy: the younger and smaller the infant, the greater the risk. In the 1960s, the rate of cerebral palsy among premature infants was around 40 percent; now it is 4–5 percent. In the IHDP, the overall rate of cerebral palsy was 4 percent. However, the children who were less than 1,500 grams had a rate of 14 percent.

Eye problems among low birthweight infants primarily involve retrolental fibroplasia, (retinopathy of prematurity), which has an incidence of about 1 percent. The incidence of sensory neural hearing loss is less than 1 percent. Premature infants are subject to serious congenital anomalies associated with low birthweight. After discharge from the hospital, these children tend to have problems of the lower respiratory tract, often requiring frequent hospitalizations during the first year of life. Once again, the smaller the infant, the larger the number of neonatal problems and the greater the complications and sequelae.

In terms of developmental issues relating to low birthweight infants, cognition is a main concern. Dunn's 1986 study tracked, for more than 6-1/2 years, a population of low birthweight infants who were 4-1/2 pounds or less. Over that period, the mean intelligence quotient (IQ) [mental developmental index (MDI)] score was 100. At 4 years of age, there was a 15-point difference (1 standard deviation) between full-term (more than 2,500 grams) infants and the premature infants, and at 6-1/2 years there was an 11-point difference. So low birthweight infants seem to have some difficulty in terms of cognition.

In terms of IQ scores in relation to birthweight, most of the early studies only followed children until they were approximately 2 years old. Over the first 2 years of life, birthweight pretty much determines a child's performance on cognitive assessments. Children who were less than 1,500 grams do the poorest, and as birthweight increases, so do IQ scores. However, after age 2, the degree of low birthweight is not an indicator of how a child performs cognitively; it only matters that a child was low birthweight.

Cognition and social class are also linked. Studies have shown that in the first 18 months, social class doesn't play a role in cognitive test performance; however, after 18 months, social class is a strong determinant of performance. Dunn's study also examined low birthweights and IQs within social classes and found some kind of cognitive disadvantage among low birthweight infants as compared with full-term infants within each class.

The school-related difficulties of low birthweight children involve reading, writing, and arithmetic. These children definitely have trouble with spatial relationships, quantitative concepts, math, etc., throughout their development. Behavioral problems of low birthweight infants manifest primarily as attention deficit disorder.

Researchers have known about these problems for some time; the question was what to do about them. Over the years, a variety of single-site, small-scale intervention studies were performed on low birthweight infants, and these resulted in short-term benefits (faster weight gain, improved interaction). On the other hand, there was also 30 years' worth of developmental studies on healthy, full-term infants who were socially disadvantaged. These studies involved programs such as Head Start, which reported long-term benefits in terms of school performance and eventual employment. So the rationale for the IHDP was based on studies both of socially disadvantaged full-term infants and of low birthweight infants.

Those designing the IHDP weren't sure whether the earlier studies would be generalizable because they were mostly small, single-site studies. They also weren't sure about the biological constraints of low birthweight infants, or how they would react in a group setting. Nevertheless, the

IHDP study was undertaken in January 1985 as a national, multisite, randomized clinical trial to determine if an intervention for these children could be evaluated. The program components consisted of a home- and center-based educational intervention program, family support services, and pediatric followup services. Eight sites were chosen from 50–60 applicant sites across the Nation. The selected sites represented a diversity of populations (e.g., the Seattle site had a large middle- and upper-middle-class population, the Miami site had a large Hispanic island population, the Texas site had a large migrant Hispanic population).

Each site was asked to bring in 135 children; one-third entered the intervention program and two-thirds went into followup. The high cost of the intervention prevented an even split. Within these groups, the children were divided into a lighter low-birthweight category (less than or equal to 2,000 grams) and a heavier low-birthweight category (2,001–2,500 grams). The designers decided to include the heavier low-birthweight category after determining that the literature on this group was very old. Nevertheless, there was some debate over whether the study should focus only on children under 1,500 grams, as these children were the main focus of previous research.

During the first year, the children received weekly home visits, and a curriculum called Partners for Learning was begun. This curriculum was used with full-term children in North Carolina who were socially disadvantaged. It consisted of a whole series of activities and exercises to engage the child, with an emphasis on social skills and language development. There were also problem-solving and social support sessions with the parents. When the children reached age 1, they entered the child development center and attended classes 5 days per week for at least 4 hours per day. In addition, parent group meetings were attended by about one-third of the parents.

The followup group was not a pure control group in that the children received health surveillance, developmental assessments, necessary medical treatment, and even interventions such as special education, if needed. The only difference between the groups was that the intervention group received very specialized, intensive educational intervention. In fact, at the end of the 3 years, over 30 percent of the children in the followup group were receiving some kind of special services in the areas at which the study was looking (i.e., cognitive development, behavior, and health).

At the end of 3 years, 93 percent of the original cohort was still involved in the study, and this percentage was the same for both the intervention and followup groups and the lighter and heavier children. This high retention rate was a credit to all the hard-working people at the sites.

### *Findings at Age 3*

Among the heavier children (more than 2,000 grams), children with the intervention had a mean IQ of 98, while the children in the followup group had a mean IQ of 85. This 13-point difference represents almost 1 standard deviation. Among the lighter children (less than or equal to 2,000 grams), the mean IQ for those with the intervention was 91, and for the followup group it was 84: a 7-point difference. In the followup group, children in both the lighter and heavier groups were at the same point cognitively, so birthweight was not an issue after a certain point in time. While neurological problems along with low birthweight can make a difference, the results for children without neurological sequelae were very consistent.

The Stanford-Binet test, which was used for this 3-year assessment, rates children who have a score of 70 or less as having mild mental retardation. Children in the followup group had an almost 3 times greater chance of having an IQ of 70 or less compared with those in the intervention.

The researchers did not expect to see any difference in behavior among the children at 3 years of age. Nevertheless, using the Achenbach Child Behavior Checklist, children in the followup group exhibited nearly twice the rate of atypical behavior (a score of 63 or higher) as those in the intervention group. This was definitely significant. The researchers tried to eradicate this difference in any way

possible, but could not.

In terms of health, the researchers were concerned that bringing children into these education center groups would compromise their health. Using a morbidity index—a cumulative index of outpatient surgeries, injuries, and minor illnesses—the researchers found that among the lighter infants those in the intervention had a higher morbidity index than those in the followup group. Looking further, the researchers found that in the first year after the children came into the center, the group of lighter infants had an average of two more doctor visits per year, and these were for minor illnesses such as respiratory infections, otitis media, and some gastrointestinal symptoms. In the second year, there was no difference between intervention and followup groups. This is a fairly common finding among normal birthweight infants; this illness among a group of children is called "herd phenomenon," and it is commonly seen in group child care situations. Other indicators of health status—including serious morbidity indexes, daily living abilities, and growth—showed no difference between the intervention and followup groups.

To summarize, the researchers saw differences in cognitive skills, behavior, and first-year health status between the followup and intervention groups. When they began analyzing this data, they were looking for a practical application. They were wondering for whom the invention worked best.

The researcher Jeanne Brooks-Gunn looked at IQ scores at 3 years of age by maternal education and race. The biggest difference was among the intervention and followup children of mothers with a high school degree or less; the intervention children scored higher than the followup group. For mothers who were college graduates, there was almost no difference between children in the two groups. So this intervention seemed to have the best result for children whose mothers had high school degrees or less.

Brooks-Gunn then analyzed the IQ scores at 3 years of age for children of mothers with high school degrees or less. Here she saw that among African Americans there was really no difference between children who were heavier or lighter in either the intervention or the followup groups. However, among white mothers, there was a difference between children who were in the intervention who weighed more than 2,000 grams and those in the followup group. There was no difference among lighter children.

Among mothers who had some college education or more, there was no difference in IQ scores between the intervention and followup groups for lighter children, either for African-American mothers or white mothers. Again, the difference was seen among heavier birthweight babies across racial groups.

### *Findings at Age 5*

This study was originally designed to provide an intervention over a 3-year period of time and measure the results; the question then became whether this intervention had any lasting effects beyond 3 years. So the researchers followed the children, assessing them at ages 5 and 8. Dr. McCarton only discussed the findings at age 5.

For children age 5, the IHDP again did very well with retention: 88 percent. The study could have increased that percentage, but it did not have enough money to visit families who could not come to one of the sites. When children were 8 years old, the study had more money for roaming assessors, and thus achieved a 90-percent followup.

At this point, Dr. McCarton noted that there were no significant differences in the baseline characteristics of children who were in the intervention and followup groups, because the children were randomized according to birthweight, sex, maternal race or ethnicity, health index, maternal education, and maternal age. These baseline characteristics remained the same throughout the study.

When the study originally ended for children at age 3, the researchers' charge was to ensure that there was no difference in the community services—child care, nursery school, Head Start,

kindergarten, or no program at all—that the children in the two groups received.

The researchers used the Wechsler Preschool and Primary Scale of Intelligence (WPPSI) to measure cognitive outcomes for children at age 5. Among the children who had been heavier low-birthweight infants, there were significant differences between the intervention and the followup groups on the full-scale WPPSI and on the verbal subscales within the test, as well as on the Peabody Picture Vocabulary Test (PPVT). (The PPVT is a receptive language scale that is different from the verbal scale on the WPPSI.) The difference between the groups amounted to a 4–5 point difference, a very modest difference, especially when compared with the 13-point differences observed at age 3. Among the lighter children, there was no difference between groups at age 5. The original 7-point difference had vanished.

The researchers saw no behavior differences among heavier and lighter infants in either group. So the behavioral differences observed at age 3 had disappeared by age 5. The same health measures were used as at age 3—the morbidity index and hospitalizations—and no differences were found between groups or weight classes.

So at age 5, after the intervention had been over for 2 years and the children had been sent out into the community, researchers found only modest differences in terms of cognitive ability (verbal IQ, full IQ, and receptive language) among heavier low-birthweight infants, and no differences at all in terms of behavior, health, and other cognitive abilities.

Brooks-Gunn examined the children's cognitive status at age 5 by maternal education. In the heavier low-birthweight children, she found that the level of maternal education had no effect, except among mothers who had some kind of college-level education. Among these mothers, there was an 8-point difference between children in the intervention group and those in the followup group. Among lighter low-birthweight infants, maternal education had no discernible effect.

There was some interest in looking at parental employment as an indicator of difference. Researchers looking at employment (defined as at least one parent employed) did see a difference in cognitive ability between the intervention and followup groups among heavier low-birthweight infants. This is because families with more money can afford more child-enrichment activities (better child care, more schooling, etc.). This is being examined further. However, there was no difference between the intervention and followup groups of heavier low-birthweight infants in families in which a parent was not employed. Among lighter low-birthweight infants, it made no difference whether a parent was employed or not.

## Conclusions

Dr. McCarton noted that this study is only the beginning, because it was designed to see whether by giving an intervention—a very intense, high-powered intervention over a long period of time—some of the problems found in low birthweight babies could be attenuated. Researchers found that this was certainly possible at age 2, but at age 5 (and at age 8) the early intervention could only achieve very modest differences among heavier low-birthweight infants in terms of cognitive ability. Among lighter birthweight infants—the infants on whom society spends the most money, the most devastated infants—the effects of the intervention are attenuated and obliterated after the intervention is stopped. Dr. McCarton said that we must now determine whether these children need longer interventions.

When this study began, some people believed that high quality care could inoculate children against the effects of premature birth, and that this inoculation would stick for life. Dr. McCarton drew an analogy with polio booster shots, and noted that while 3 years is a long period of time for an intervention, it is not a long period of time in the life of the children. They go home to environments that are very different from the intervention centers.

Dr. McCarton said that researchers must now look at more appropriate interventions for the lighter low-birthweight infants, as well as at the intensity of the intervention and when it should start. A whole new set of studies must come forth from this.

## Reaction

Dr. Bauchner opened his reaction by commenting that there has been a handful of landmark studies in pediatrics in the United States, and this is one of them. This study is important because premature infants are estimated to consume 20–40 percent of the health care dollars for pediatrics in the Nation (the range depends on whether social costs are included or not), and because the study involved a randomized clinical trial. He suggested that pediatric researchers need to increase the number of randomized clinical trials they perform. He did note in his opening remarks the high cost of the study and asked whether the results, to date, were disappointing.

He noted that there is much more analysis yet to be done with this cohort. First, this study has demonstrated that a second inoculum maybe necessary. It is quite possible that the intervention from birth to age 3 years was not sufficient. Second, there are likely to be "sleeper" effects—unexpected impacts of the intervention—further down the line. The question is whether the researchers can identify them. The gains in IQ points are very minimal. At 8 years and beyond, researchers need to focus on school achievement and social functioning among the groups, and here again this study has an advantage over older studies because it was a randomized clinical trial.

In terms of improving the design of future studies, Dr. Bauchner stated that the coding of race/ethnicity (black, white, Hispanic) no longer holds in the 1990s. If this study is ever done again, the coding of race/ethnicity would have to be much different.

Dr. Bauchner said that in designing a randomized clinical trial, researchers can do an extreme intervention—and then, if it works, they can speculate on whether less intervention would have worked—or they can do a practical intervention. This was a "Mercedes" intervention, and it was not subjected to a cost analysis. Given cost containment, managed care, and decreased funding for social care, it is difficult to imagine a future "Mercedes" intervention such as this. Dr. Bauchner said that more exploratory studies are needed to determine what reasonable intervention could be provided to the families of the lighter infants. Dividing the data at the end into variables that cannot be changed is frustrating to the consuming public. Such variables as the mother's high school degree cannot be changed after a child is born; variables that can be changed might be more helpful.

In summary, Dr. Bauchner said that some cost analysis of the intervention was needed. Long-term sleeper effects could help justify some of the cost. Finally, a parental evaluation of the intervention would be very helpful and is frequently ignored in studies of this type. Even now, 8 years later, the parents could be asked what it meant to them to participate in the study. Their responses may help design a more targeted, effective intervention in the future.

Discussion questions centered on the length of the study and the effects of changing medicine over that period of time, social class variables, the effects of Head Start, long-term followup of the children, the cost of the study, parental participation, socialization of the children in the followup study, the convergence of IQ scores among the groups, the difficulty of surveying the children's schools, the intensity of the intervention, the purity of the followup group, and the single-blind nature of the study.

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